AMENDMENTS

Amendments to the Specification:

Please amend paragraph 0025 as follows:

[0025] A genetic analysis provided herein linked melanoma with polymorphic variants of a nucleotide sequence located on chromosome seven that encodes a serine/threonine protein kinase polypeptide designated BRAF. The BRAF gene is located on chromosome 7q34 (assembly 30), and covers approximately 190 kb. It contains at least 19 exons and encodes a full-length transcript of 2510 bp (NM_004333). At least seven variant transcripts have been identified, which are the product of alternative splicing. From these various transcripts, several proteins are translated, including the full-length, 94-95 kD, 783 amino acid product (see World Wide Web ~~http~~ address at ncbi.nlm.nih.gov/LocusLink/).

Please amend paragraph 0082 as follows:

[0082] Comparison of sequences and determination of percent identity between two sequences can be accomplished using a mathematical algorithm. Percent identity between two amino acid or nucleotide sequences can be determined using the algorithm of Meyers & Miller, CABIOS 4: 11-17 (1989), which has been incorporated into the ALIGN program (version 2.0), using a PAM120 weight residue table, a gap length penalty of 12 and a gap penalty of 4. Also, percent identity between two amino acid sequences can be determined using the Needleman & Wunsch, J. Mol. Biol. 48: 444-453 (1970) algorithm which has been incorporated into the GAP program in the GCG software package (available at the World Wide Web ~~http~~ address gcg.com), using either a Blossum 62 matrix or a PAM250 matrix, and a gap weight of 16, 14, 12, 10, 8, 6, or 4 and a length weight of 1, 2, 3, 4, 5, or 6. Percent identity between two nucleotide sequences can be determined using the GAP program in the GCG software package (available at World Wide Web ~~http~~ address

gcg.com), using a NWSgapdna.CMP matrix and a gap weight of 40, 50, 60, 70, or 80 and a length weight of 1, 2, 3, 4, 5, or 6. A set of parameters often used is a Blossum 62 scoring matrix with a gap open penalty of 12, a gap extend penalty of 4, and a frameshift gap penalty of 5.

Please amend paragraph 0085 as follows:

[0085] BRAF nucleotide sequences and polypeptide sequences can be used as "query sequences" to perform a search against public databases to identify other family members or related sequences, for example. Such searches can be performed using the NBLAST and XBLAST programs (version 2.0) of Altschul et al., J. Mol. Biol. 215: 403-10 (1990). BLAST nucleotide searches can be performed with the NBLAST program, score = 100, wordlength = 12 to obtain nucleotide sequences homologous to BRAF nucleic acid molecules. BLAST polypeptide searches can be performed with the XBLAST program, score = 50, wordlength = 3 to obtain amino acid sequences homologous to BRAF polypeptides. To obtain gapped alignments for comparison purposes, Gapped BLAST can be utilized as described in Altschul et al., Nucleic Acids Res. 25(17): 3389-3402 (1997). When utilizing BLAST and Gapped BLAST programs, default parameters of the respective programs (e.g., XBLAST and NBLAST) can be used (see the World Wide Web ~~http~~ address ncbi.nlm.nih.gov).

Please amend paragraph 00235 as follows:

[00235] RNAi-based gene inhibition is a rapid way to inhibit expression of BRAF in cultured cells. siRNA reagents were selectively designed to target BRAF. Algorithms useful for designing siRNA molecules specific for BRAF are disclosed at the World Wide Web ~~http~~ address dhramacon.com. siRNA molecules up to 21 nucleotides in length are utilized. Table 22 summarizes the features of the duplexes that may be used in the assays described herein, where the sequence of one strand is shown (the other strand is complementary). A non-homologous siRNA reagent is used as a negative control.